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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,425	02/12/2004	Paul R. Sanberg	1372.129.PRC	4329

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EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
12/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/777,425	SANBERG ET AL.	
	Examiner	Art Unit	
	TAEYOON KIM	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-12 and 14-26* is/are pending in the application.

4a) Of the above claim(s) *19-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-12 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response filed on 8/31/2009 has been received and entered into the case.

Claims 19-26 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 1, 5-12 and 14-18 have been considered on the merits. All arguments have been fully considered.

The claim rejection under 35 U.S.C.§112 has been withdrawn due to the amendment.

The claim rejection under 35 U.S.C.§102 has been withdrawn due to the amendment.

The amendment made to the specification is accepted and entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 5-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 discloses a new limitation of "generating myocytes and further comprising administering … umbilical cord blood cell…" It is not clear whether the method step of generating myocytes is an independent and separate step from the method step of administering umbilical cord blood cell, and thus requires in vitro or ex vivo step of generating myocytes from any source, or the myocytes are formed from the umbilical cord blood cells in vivo by the administering step. Clarification is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5-12 and 14-18 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Pittenger et al. (of record) in view of Dengler et al. (of record) in further view of Edelberg et al. (of record), Isner et al. (of record), Erices et al. (of record) and Lim et al. (of record).

Pittenger et al. teach a method of regenerating cardiac muscle using mesenchymal stem cells (MSCs) (see abstract). Pittenger et al. teach human MSCs being introduced to the infarct zone (myocardial infarction; cardiac injury) to reduce the degree of scar formation and to augment ventricular function (treating a circulatory disorder; col. 4, lines 7-19). Pittenger et al. also teach direct or systemic administration (col. 2, lines 25-30) and an amount of cells for administration being 10-40x10^6 MSCs/ml (col. 4, lines 65-67).

Although Pittenger et al. do not teach umbilical cord blood cells used in the method, it would have been obvious to a person of ordinary skill in the art to substitute MSCs of Pittenger with UCBCs. This is because Dengler et al. teach that UCBCs comprise stem cells with a capability of differentiating into cardiac myocytes (p.604, right col. under "umbilical cord stem cells"), Edelberg et al. teach that endothelial progenitor cells, which can also differentiate into cardiomyocytes, are also present in UCB (par. 18 and 24), and Isner et al. teach the use of endothelial progenitor cells derived from UCB in treating of cardiovascular disorder and therefore, a person of ordinary skill in the art would recognize suitability of UCBCs an

alternative to MSCs of Pittenger et al. in the method of treating cardiovascular dysfunctions.

M.P.E.P. §2144.07 states "The selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945) (Claims to a printing ink comprising a solvent having the vapor pressure characteristics of butyl carbitol so that the ink would not dry at room temperature but would dry quickly upon heating were held invalid over a reference teaching a printing ink made with a different solvent that was nonvolatile at room temperature but highly volatile when heated in view of an article which taught the desired boiling point and vapor pressure characteristics of a solvent for printing inks and a catalog teaching the boiling point and vapor pressure characteristics of butyl carbitol. "Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle." 325 U.S. at 335, 65 USPQ at 301.)".

Although Dengler et al. do not particularly teach that UCBCs are mesenchymal cells, it is well known in the art that UCBCs comprises mesenchymal progenitor cells according to Erices et al. Therefore, the UCBCs of Dengler et al. inherently comprise mesenchymal cells.

Although Pittenger et al. in view of Dengler et al. and Edelberg et al. do not teach the limitation of administering the UCBCs within approximately 48 hours after the onset of myocardial infarction, a person of ordinary skill in the art would recognize that the range of hours for administration of UCBCs is a result-effective variable. As such, the variables would be routinely optimized by one of ordinary skill in the art in practicing the invention disclosed by those references. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such

concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); >see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); ** In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). Accordingly, the claimed invention was prima facie obvious to one of ordinary skill in the art at the time the invention was made especially in the absence of evidence to the contrary.

With regard to the limitation of the umbilical cord blood composition comprising at least 6 million white blood cells per milliliter, the use of UCBCs in a method of treating myocardial infarction as taught by Pittenger et al. in view of Dengler et al. in further view of Edelberg et al. inherently meets the limitation of the white blood cell contents, since Lim et al. teach that UCB

contains about 11 million white blood cells per ml (see Table 1).

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Applicant's arguments filed 8/30/2009 have been fully considered but they are not persuasive.

Applicant alleged that the references do not provide for the treatment of circulatory disorder by generating myocytes, which is a new limitation added in the instant amendment. Unlike the allegation, Dengler et al. clearly teach that umbilical cord blood cells containing stem cells can differentiate into cardiac myocytes (p.604, right col. under "umbilical cord stem cells")

Applicant also argued that the composition must be administered to infarcted regions to generate myocytes, and the teaching of Dengler et al. do not administer UCBC to infarcted regions.

It is understood that claim 9 discloses that the injection is made directly to heart tissue, and this disclosure might be considered what applicant alleged that the invention requires administration of the cells into the infarcted regions. However, it is clearly disclosed in claim 10 that the administration can be carried out systemically. Thus, the claimed method does not particularly require injection of the cells into the infarcted area.

Further, Dengler et al. show various different routes of administration including infarct area as shown in Fig. 1.

Although applicant cited a reference by Kern, without a copy provided to the Office, this argument is not considered. Nevertheless, the argument that the art does not recognize the

capacity for MSC to generate cardiomyocytes is not correct considering the teaching of Pittenger et al. as well as Dengler et al.

Applicant asserted that the OA did not provide a rationale why the stem cells of Dengler et al. would be recognized as a suitable replacement for MSCs of Pittenger. This argument is not persuasive. As applicant argued, MSCs of Pittenger is from bone marrow, and the purpose of the cells in the method of Pittenger is to regenerate cardiac muscle based on the fact that MSCs differentiate into cardiomyocytes. Dengler et al. provide various different cell types capable of producing cardiomyocytes including MSCs from bone marrow and UCBC stem cells. Thus, it would have been obvious to a person of ordinary skill in the art that MSCs from bone marrow share the same functionality with UCBC stem cells in differentiating into cardiomyocytes. Thus, it is clear that UCBC stem cells are art-recognized alternative to MSCs of bone marrow in the method of Pittenger.

It is noted that Isner et al. is not disclosed as a part of claim rejection while it is discussed in the rejection. It is regretted that Isner et al. was inadvertently omitted from the first sentence of the claim rejection. The deficiency has been corrected.

The teaching of Isner et al. combined with Pittenger et al. is that the use of UCBC for treatment of cardiac conditions.

Applicant argued that the combination of the teaching of Isner et al. with Pittenger et al. changes the principle operation of a reference. This assertion is based on the purpose of Pittenger is to regenerate cardiac muscle whereas the purpose of Isner et al. is to enhance angiogenesis, and thus, changes the principle operation.

It is submitted that UCBC contains not only endothelial cell progenitors but also stem cells capable of differentiating into cardiomyocytes. As disclosed by Isner et al., UCBC is a source of EC progenitors, and also as disclosed by Dengler et al. UCBC is a source of stem cells capable of differentiating into cardiomyocytes. Therefore, the use of UCBC in the method of Pittenger et al. does not change the principle of operation of Pittenger et al. since stem cells present in UCBC capable of differentiating into cardiomyocytes would inherently generate cardiomyocytes in addition to enhance angiogenesis by EC progenitors.

Therefore, the applicant's argument is not sufficient to overcome the claim rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5-8, 10-12 and 15-17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending

Application No. 12/117,197 in view of Dengler et al. (of record). The claims of '197 application anticipate the claimed subject matter of the current application. Although they are not identical, the claims of '197 are directed to a method of treating myocardial infarction by administering human umbilical cord blood cells, and these are same as the claimed method of the instant application. Although the claims of '197 do not particularly teach that the UCBC differentiate into cardiomyocytes after transplantation, it is considered as an inherent property of UCBC to differentiate into cardiomyocytes according to Dengler et al.

This is a provisional obviousness-type double patenting rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TAEYOON KIM whose telephone number is (571)272-9041. The examiner can normally be reached on 8:00 am - 5:00 pm ET (Mon-Thu).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taeyoon Kim/
Primary Examiner, Art Unit 1651